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Date: September 22, 2003

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To: Masaharu Ishikawa
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Facsimile No: 011-81-3-3499-6152

From: Karen L. Elbing, Ph.D.

Re: EXPRESSION OF XENOGENOUS (HUMAN)
IMMUNOGLOBULINS IN CLONED, TRANSGENIC
UNGULATES
U.S. Patent Application No. 09/988,115
Our Reference: 50195/008003

Pages: 10 pages

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SEP 2 3 2003

EXPRESSION OF XENOGENOUS (HUMAN) IMMUNOGLOBULINS IN
CLONED, TRANSGENIC UNGULATES

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Dear Jim and Dr. Ishikawa:

We have received the attached Restriction Requirement in which the Examiner has divided the claims into the following separate groups:

- | | | |
|-----------|-----------------------|--|
| Group I | Claims 1-19 and 21-29 | Transgenic ungulates or ungulate somatic cells comprising one or more nucleic acids encoding a xenogenous immunoglobulin gene which undergoes rearrangement; |
| Group II | Claim 20 | A hybridoma expressing a xenogenous Ig molecule; |
| Group III | Claims 30-38 | Method of producing transgenic ungulates by transfer of a cell, or its chromatin mass or nucleus, into an oocyte, wherein the cell comprises a mutation in an endogenous antibody heavy chain or light chain nucleic acid; |
| Group IV | Claim 42 | Method of producing transgenic ungulates comprising inserting into an oocyte a cell, or its chromatin mass or nucleus, where the cell |

comprises a mutation in an endogenous antibody gene;

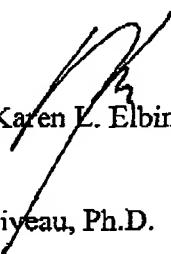
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|------------|------------------|---|
| Group V | Claim 43 | A method of producing transgenic ungulates comprising inserting into an oocyte a cell, or its chromatin mass or nucleus, where the cell comprises a mutation in an endogenous α -1,3-galactosyltransferase gene; |
| Group VI | Claim 44 | Method of producing transgenic ungulates comprising inserting into an oocyte a cell, or its chromatin mass or its nucleus, where the cell comprises a mutation in an endogenous prion gene; |
| Group VII | Claims 45 and 46 | Method of producing transgenic ungulates comprising inserting into an oocyte a cell, or its chromatin mass or nucleus, where the cell comprises a mutation in an endogenous J gene or a nucleic acid encoding a J gene; |
| Group VIII | Claim 47 | Ungulate serum comprising human polyclonal immunoglobulins; and |
| Group IX | Claim 48 | Ungulate milk comprising human polyclonal immunoglobulins. |

The deadline for replying to this Restriction Requirement, which involves choosing one of these groups for initial examination, is OCTOBER 11, 2003, with extensions available to March 11, 2004 upon payment of fees. With your instructions, kindly also let us know whether you wish, for the record, to disagree with the Examiner's claim groupings.

We note that more than one group can be chosen for examination at this time simply by filing one or more divisional applications.

Please feel free to contact me or Michael Belliveau if you have any questions.

Very truly yours,


Karen L. Elbing, Ph.D.

Enclosure

cc w/o enc.: Michael J. Belliveau, Ph.D.